

Abnormalities of the uterine cervix in women with vulval warts

A preliminary communication

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SUMMARY Fifty women attending a clinic for sexually transmitted diseases with vulval condylomata acuminata were examined by cervical cytology and colposcopy for cervical infection by human papillomavirus (HPV) or epithelial abnormality indicating cervical intraepithelial neoplasia (CIN) or both. Collated results showed a high prevalence of both conditions in these 50 women; 25 (50%) had evidence of cervical infection by HPV and 18 (36%) epithelial abnormalities consistent with CIN 1 or 2.

Introduction

Genital warts have been well known for many centuries. The most usual form on the penis and the vulva is the fleshy condyloma acuminatum, but common and plane warts may also occur.¹ Papillomavirus particles are seen by electron microscopy at low concentrations in about 50% of extracts of genital warts,² and recent studies have shown that a human papillomavirus (HPV) of distinctive subtype (HPV-6) is present in the lesions.³

In recent years interest in cervical disease associated with HPV infection has been growing. Condyloma acuminatum of the cervix (exophytic condyloma) is a familiar condition; it is associated with the characteristic cytological findings of koilocytosis, dyskeratosis, and nuclear atypia.⁴ It is now apparent that these findings are present in many women who do not have exophytic condylomata. In these women condyloma acuminatum is associated with inconspicuous cervical lesions which are visible only by colposcopy. These lesions have been called flat condylomata, and their viral aetiology is in no doubt. Histologically they resemble warts at an early stage of development⁵; by electron microscopy they contain papillomavirus particles,⁶ and hybridisation studies indicate that this virus is usually of the subtype HPV-6.⁷

Flat condylomata have also been described as non-condylomatous cervical wart virus infection⁸ or as subclinical papillomavirus infection,⁹ terms which indicate their essentially non-papilliferous nature. In the past they were usually classified cytologically and colposcopically as cervical intraepithelial neoplasia (CIN).⁴ Papillomavirus infection of the cervix is much commoner than had previously been suspected, occurring in as many as 1% of unselected cervical smears from some populations.⁵⁻⁸ The disease may appear alone or in association with vulval or cervical condyloma acuminatum or both, but the relationship between the vulval and cervical lesions is not yet clear.

Genital warts are common in women who attend clinics for sexually transmitted diseases (STD). In England the disease is reportable and in 1980 was diagnosed in 10 246 women.¹⁰ Previous studies¹ have reported that exophytic condylomata are present in up to 6% of women with vulval warts, but the incidence of other types of cervical disease due to HPV is not known. The purpose of this investigation was to study a group of women attending a clinic for STD with vulval warts, to seek evidence of cervical disease which might be due to wart virus infection, and to investigate its natural history.

Patients and methods

All the patients attended the department of genitourinary infection, University College Hospital, between December 1981 and May 1982. They had vulval warts which had been diagnosed clinically;

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vulval biopsy was not performed. Women who attended as contacts of men with gonorrhoea or non-gonococcal urethritis were excluded, but otherwise they were unselected. All the patients gave their consent to participate in this study, which had been approved by an ethics committee.

For each patient age, age at the time of first intercourse, lifetime number of sexual partners, and the duration of the vulval warts were recorded. A general medical history was also taken. The women were examined in the lithotomy position, and vaginal, cervical, and anal condylomata or other abnormalities were carefully looked for. Specimens were collected from the urethra and cervix for the identification of *Neisseria gonorrhoeae*, from the cervix only for culture for *Chlamydia trachomatis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, and herpes simplex virus, and from the posterior vaginal fornix for the identification of *Trichomonas vaginalis*, *Gardnerella vaginalis*, and *Candida* spp. Standard procedures were used for the identification of these organisms in the laboratory.¹¹ Serological tests for syphilis were also performed. Cervical cytology was undertaken by standard techniques.¹²

Colposcopy was performed on all patients using a Zeiss OPMI-1 instrument. The cervix was visualised with a vaginal speculum and examined at $\times 6.4$ and $\times 10$ magnification unstained and after washing firstly with 5% aqueous acetic acid solution then with Lugol's iodine. Cervical biopsy was not performed as a routine, as our study of the course of untreated HPV infection of the cervix might have been prejudiced by this procedure. If, however, cervical cytology or colposcopy identified an abnormal epithelium consistent with a diagnosis of CIN 3, the patient was removed from the study and referred to a department of gynaecology for further investigation and treatment.

Results

Fifty women with vulval warts were studied; demographic and sexual data are shown in table I

TABLE I Demographic and sexual data on women with vulval warts (n = 50)

	Range	Mean
Present age (years)	17-31	24
Age of first coitus (years)	15-24	17
Lifetime number of sexual partners	1-66	9
Period of coitus (years)	3m-16	6
Duration of vulval warts (weeks)	1-80	16

TABLE II Associated infections in women with vulval warts (n = 50)

Organism	No positive/No of specimens	% Positive
<i>N gonorrhoeae</i>	0/50	0
<i>C trachomatis</i>	4/47	8.5
<i>M hominis</i>	17/45	37.8
<i>U urealyticum</i>	32/45	71.1
<i>G vaginalis</i>	9/48	18.8
<i>T vaginalis</i>	2/50	4.0
Herpes simplex virus 2	2/49	4.1
<i>Candida</i> spp	13/50	26.0

and the associated infections present in table II. Serological test results for syphilis were negative in all patients.

CERVICAL CYTOLOGY

In 14 cases the cervical smears were inadequate for reporting because they did not contain endocervical or metaplastic squamous cells. This criterion was strictly applied, even if the material present showed some cellular abnormality. Two smears which showed gross cellular changes due to *T vaginalis* infection could not be assessed for concomitant wart virus atypia. Valid results were therefore available for 34 women (table III).

Cytological evidence of wart virus infection was present in eight (23.5%) of the 34 specimens, of cellular abnormality consistent with CIN 1 in four, and of wart virus infection together with CIN 1 in two. Thus, of the 34 smears from women with vulval

TABLE III Results of cervical cytology and colposcopy in 50 women with vulval warts

Findings	Cervical cytology (n = 34 smears)	Colposcopy (n = 50 examinations)
No with evidence of:		
CIN 1/2	4	8
CIN 1/2 and wart virus infection	2	9
Wart virus infection alone	8	11
Total No (%) with evidence of:		
CIN 1/2	6 (18)	17 (34)
Wart virus infection	10 (29)	20 (40)
Any abnormality	16 (41)	28 (56)

CIN = cervical intraepithelial neoplasia

warts six (18%) indicated CIN 1 and 10 (29%) wart virus infection. When the prevalence of CIN and of wart virus infection in this group is compared with that in three other groups of patients—women attending our department who did not have vulval warts, women attending a nearby family planning clinic, and women examined in a gynaecological outpatient clinic at University College Hospital (table IV)—the proportion of patients with cytological evidence not only of wart virus infection but of CIN was greatest in the women with vulval warts.

COLPOSCOPY

Of the 50 women with vulval warts, abnormal acetowhite epithelium consistent with a diagnosis of wart virus infection was the sole abnormality in 11, epithelium consistent with CIN 1 or 2 was present in eight, and colposcopic evidence of wart virus infection together with CIN 1 or 2 was found in nine (table III). Altogether, 20 (40%) of the 50 women with vulval warts had cervical changes indicative of wart virus infection; six had exophytic condylomata, but the remaining 14 had no evidence of wart virus infection by naked eye examination of the cervix.

COMPARISON OF CYTOLOGY AND COLPOSCOPY

In this study the results of cervical cytology and colposcopy for the diagnosis of wart virus infection were not in close agreement. There was cytological evidence of wart virus infection as the sole abnormality in eight cases, but this was confirmed by colposcopy in only four. Conversely, in seven women with colposcopic evidence of wart virus infection as the sole abnormality in whom valid cytology was available confirmation was possible in only three. We speculate that a colposcopic diagnosis of wart virus infection which is unsupported by cytology may be due to inadequate sampling of the whole transformation zone; on the other hand, a cytological diagnosis of wart virus infection unsupported by colposcopy could be explained by the existence of early papillomavirus infections which are producing changes at only cellular level. These hypotheses might have been confirmed by cervical biopsy and histology, but this was not performed for reasons already given.

Discussion

Many of the women with vulval warts had an associated lower genital tract infection. The prevalence of infection with *N gonorrhoeae* and *C trachomatis* was relatively low because sexual contacts of men with gonorrhoea or non-gonococcal urethritis were excluded from the study. The prevalence of the other micro-organisms was similar to that found in the total clinic population.

Clearly, there was a substantial amount of cervical abnormality among the women with vulval warts whom we studied. Collated results from cervical cytology and colposcopy showed that 16% of these women had evidence of minor degrees of CIN, 30% evidence of wart virus infection alone, and 20% evidence of both conditions. The criteria for distinguishing between CIN and wart virus infection by colposcopy were those of Reid *et al.*⁸ Recently, it has been suggested that such a fine distinction cannot be made with the colposcope.¹³ Nevertheless, in a parallel study of 48 patients in whom we made a colposcopic diagnosis of wart virus infection this was confirmed by histology in 40 (83%), which implies that the colposcope can be a relatively accurate tool in this context.

There has been much discussion of the possible role of sexually transmitted agents, such as herpes simplex virus and HPV, in the natural history of CIN. It is known that CIN is related epidemiologically to early age of first sexual intercourse and multiple sexual partners; the results of the present study showed that patients with vulval warts may share these epidemiological features. The relationship between wart virus infection and CIN, however, remains uncertain. They may represent conditions which are simply covariables of promiscuity, but evidence is accumulating which suggests that HPV may have a causal role in the development of CIN and cervical cancer, acting either alone or in association with other agents. No doubt the truth will emerge after further research. In the mean time the fact that a high proportion of women with vulval warts also have cytological and colposcopic evidence of wart virus infection and of

TABLE IV *Cervical cytology results in women attending outpatient clinics*

Source	No of patients	No of patients with valid smears	Cytology findings (%):		
			CIN I	Wart virus infection	Any abnormality
STD clinic					
Vulval warts	50	34	17.7	29.4	41.2
No vulval warts	100	85	8.2	1.2	8.2
Family planning clinic	100	94	3.3	0.0	3.3
Gynaecology clinic	100	89	1.1	0.0	1.1

CIN must mark them out as a group requiring special attention. Prospective studies of the natural history of these lesions may show that many regress spontaneously, though if untreated some will develop into carcinoma in situ or even invasive cancer over several years. Care should, therefore, be taken to obtain adequate cervical smears from women attending STD clinics with vulval warts and possibly also from female sexual partners of men with penile condylomata. Persistently abnormal cytological findings suggest that the patient should be referred for colposcopy.

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